HAE with normal C1-INH: Treatment and attack frequency based on data from the Canadian 2020 national survey

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Abstract

Introduction: Hereditary angioedema with normal C1-esterase inhibitor (HAEnC1-INH) is associated with mutations in Factor XII and other genes. In the absence of genetic testing, diagnosis is based on clinical symptoms of angioedema and normal C1-INH functional levels so medication access can be difficult and available medications may not be fully effective.

Methods: In 2020, an online survey was sent to all members of HAE Canada. Survey results were collated and sorted by self-reported HAEnC1-INH and Type 1/2 HAE. Demography, medication use and angioedema attacks are reported and expressed as percent of respondents.

Results: Forty-five adult patients (84% female) with HAEnC1-INH and 106 (76% female) with Type 1/2 HAE responded to the survey. For the prior year, more respondents with HAEnC1-INH reported ≥12 angioedema attacks (50% vs 27%) and fewer reported having none (10% vs 21%) compared to those with Type 1/2 HAE. Laryngeal attacks were experienced by 43% with HAEnC1-INH versus 24% with Type 1/2 HAE.

Most respondents indicated that their primary treatment for acute attacks (HAEnC1-INH 41%, Type 1/2 HAE 59%) and prophylaxis (HAEnC1-INH 45%, Type 1/2 HAE 59%) was plasma-derived (pd) C1-INH. Others used icatibant to treat acute attacks (HAEnC1-INH 30%, Type 1/2 HAE 23%).

Discussion: These results suggest pdC1-INH is used to treat a large proportion of patients with HAEnC1-INH despite presumed normal C1 inhibitor function. Half experience >12 attacks per year and 43% have laryngeal attacks - higher than those with HAE Type 1/2. In Canada, new treatments targeting angioedema, genetic testing and precision medicine are needed for HAEnC1-INH patients.

Introduction

Hereditary angioedema (HAE) is a rare inherited disorder characterized by recurrent painful episodes of severe swelling in different parts of the body. C1-esterase inhibitor (C1-INH) activity is impaired in the majority of patients, but a subset of patients exhibit the same symptoms despite normal C1-INH (HAEnC1-INH). In the absence of genetic testing, diagnosis is based on history and clinical presentation. Moreover, there are no approved treatments for these patients. As a result, access to treatment can be problematic and medications approved for HAE may not be fully effective.

Objective

We sought to understand what medications patients with HAEnC1-INH use to treat their angioedema and how effective these medications are.

Methods

In 2020 a comprehensive email survey was sent to all members of HAE Canada to gather information on multiple aspects of HAE. The data from respondents was collected and analysed as the percentage of respondents to that question. Responses to 4 questions on medication use and attack rates were analysed for this report.

Results

The survey collected data from 209 respondent adults living with HAE. Of these, 106 (76% female) had Type I or Type II HAE and 45 (84% female) had HAE with normal C1INH.

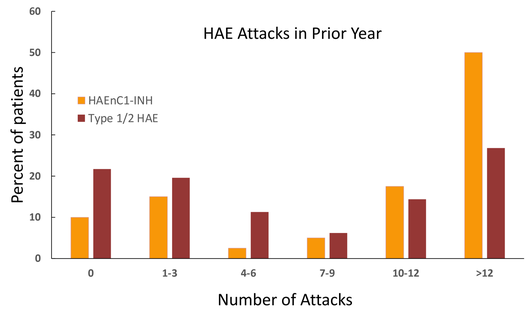

Figure 1. Yearly HAE attacks were more frequent for patients with HAEnC1-INH (n=40); 73% had 7 or more compared to only 47% of Type 1/2 (n=97) patients. Twice as many Type 1/2 patients were attack free.

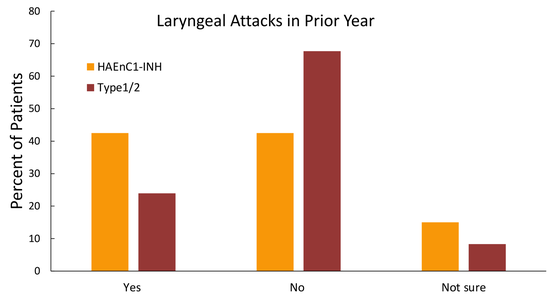

Figure 2. In response to the question "*Have you ever had a laryngeal attack in the past year?"* The majority of Type 1/2 patients (65/96, 68%) answered No compared to only 42% (17/40) of HAEnC1-INH patients.

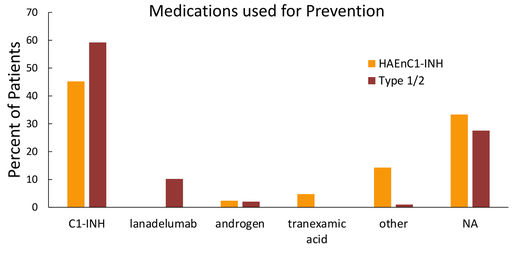

Figure 3. Type 1/2 and HAEnC1-INH patients predominantly used pdC1-INH for long-term prophylaxis (59 and 45%, respectively). Lanadelumab was used exclusively by Type 1/2 patients and tranexamic acid exclusively by HAEnC1-INH patients. A slightly higher proportion of patients with HAEnC1-INH were not using medication for long-term prevention (33% vs 28%). Other includes prednisone, montelukast, IgG replacement therapy, pain medication and cannabis.

Results (continued)

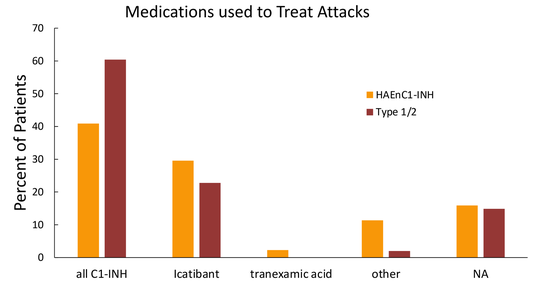

Figure 4 Type 1/2 (n=101) and HAEnC1-INH (n=44) patients predominantly used pdC1-INH to treat acute attacks (60 and 41%, respectively). 23% of Type 1/2 and 30% of HAEnC1-INH patients treated acute attacks with icatibant while tranexamic acid was used exclusively by those with HAEnC1-INH. The proportion of patients not using treatment to treat attacks was similar for both groups (16% vs 15%). Other included diazepam, pain medication, steroids, epinephrine autoinjector and antihistamine.

Conclusions

- Our results suggest that pdC1-INH is used to treat patients with HAEnC1-INH despite presumed normal C1 inhibitor function.
- Icatibant, a bradykinin receptor antagonist is used to treat acute attacks in a subset of patients of both types.
- About 1/3 of patients do not use any treatment to prevent attacks and about 15% do not use rescue therapy to treat attacks.
- Patients with HAEnC1-INH experienced more frequent attacks in the preceding year including laryngeal attacks than those with Type1/2 HAE.
- In Canada, new treatments targeting angioedema, genetic testing to make or confirm diagnosis and precision medicine are needed for HAEnC1-INH patients.

Acknowledgements

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